

METHODS AND COMPOUNDS FOR MODULATING MALE FERTILITY

Cross Reference To Related Applications

5 This application claims priority from co-pending U.S. Utility
Application Serial No. 09/239,867, filed January 29, 1999, which claims benefit
from U.S. Provisional Application Serial No. 60/073,001, filed January 29, 1998
(now abandoned). now US. Pat. No. 6,331,412 ✓

Background of the Invention

10 The invention relates to apoptosis in cells, particularly cell involved in
fertility.

15 Apoptosis is a fundamental process of cell death required for the
elimination of unwanted cells in multicellular organisms and involves an ordered
cascade of events leading to hallmark morphological changes including nuclear
condensation, chromosome laddering, and membrane blebbing. In one specific
example, apoptosis plays a prominent role during all stages of sperm development.
Spermatogenesis is a process that results in the generation of mature sperm cells
from primary germ cells, and some of the events affected by apoptosis include the
elimination of unwanted cells and the prevention of the death of those cells
20 destined to become functional sperm (Hsueh *et al.*, Recent Prog. Horm. Res. 51:
433, 1996; Furuchi *et al.*, Development 122: 1703, 1996).

25 Much of the current knowledge of the biochemical pathways involved
in apoptosis comes from the study of viruses. The baculoviral proteins involved in
apoptosis, CpiAP and OpiAP, are characterized by two amino terminal cys/his
motifs (Xaa₃-R-Xaa₂₀₋₂₃-G-Xaa₁₁-C-Xaa₂-C-Xaa₁₆-H-Xaa₆-C-Xaa₃) (SEQ ID NOs:
6-9) and a carboxy terminal C-Xaa₂-C-Xaa₁₁-C-Xaa-H-Xaa₃-C-Xaa₂-C-Xaa₆-C-
Xaa₂-C RING zinc finger motif (SEQ ID NO: 10) reviewed in Clem *et al.*, Cell